

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF THE CLAIMS

1. (Withdrawn) A pharmaceutical composition comprising a therapeutically effective amount of a tissue protective cytokine; at least one anti-inflammatory agent; and a pharmaceutically acceptable carrier.

2. (Withdrawn) The pharmaceutical composition of claim 1, wherein the anti-inflammatory agent is selected from the group consisting of corticosteroids, glucocorticoids, steroids, non-steroidal anti-inflammatory drugs, beta-agonists, anticholinergic agents, methyl xanthines, gold injections, sulphasalazine, penicillamine, anti-angiogenic agents, dapsone, psoralens, anti-malarial agents, anti-viral agents, and antibiotics.

3. (Withdrawn) A pharmaceutical composition comprising a therapeutically effective amount of a tissue protective cytokine; at least one immunomodulatory agent; and a pharmaceutically acceptable carrier.

4. (Withdrawn) The pharmaceutical composition of claim 3, wherein the immunomodulatory agent is selected from the group consisting of methotrexate, leflunomide, cyclophosphamide, cytoxin, Immuran, cyclosporine A, minocycline, azathioprine, antibiotics, methylprednisolone, corticosteroids, steroids, mycophenolate mofetil, rapamycin, mizoribine, deoxyspergualin, brequinar, malononitrioloamides, T cell receptor modulators, and cytokine receptor modulators.

5. (Withdrawn) A pharmaceutical composition of claim 1 or 3, wherein said tissue protective cytokine is selected from the group consisting of i) an erythropoietin that lacks sialic acid moieties; ii) an erythropoietin that lacks N-linked or lacks O-linked carbohydrates; iii) an erythropoietin having a reduced carbohydrate content by treatment of native erythropoietin with at least one glycosidase; iv) an erythropoietin having at least one or more oxidized carbohydrates; v) an erythropoietin comprising at least one or more oxidized carbohydrates which is chemically reduced; vi) an erythropoietin comprising at least one or more modified arginine residues; vii) an erythropoietin comprising at least one or more modified lysine residues or a modification of the N-terminal amino group of the erythropoietin molecule; viii) an erythropoietin comprising at least a modified tyrosine

residue; ix) an erythropoietin comprising at least a modified aspartic acid or a glutamic acid residue; x) an erythropoietin comprising at least a modified tryptophan residue; xi) an erythropoietin having at least one amino group removed; xii) an erythropoietin comprising at least an opening of at least one of the cystine linkages in the erythropoietin molecule; and xiii) a truncated erythropoietin.

6. (Cancelled).

7. (Cancelled).

8. (Currently amended) A method for treating inflammation in a mammal comprising responsive cells, ~~tissues, and/or organs~~, said method comprising administering to a mammal in need thereof a pharmaceutical composition comprising a prophylactically or therapeutically effective amount of a tissue protective cytokine and a pharmaceutically acceptable carrier, and administering to the mammal a prophylactically or therapeutically effective amount of one or more anti-inflammatory agents or immunomodulatory agents.

9. (Currently amended) The method of claim 8, wherein the anti-inflammatory agent is selected from the group consisting of a corticosteroid, a glucocorticoid, a steroid, a non-steroidal anti-inflammatory drug, a beta-agonist, an anticholinergic agent, a methyl xanthine, gold injection, a sulphasalazine, penicillamine, an anti-angiogenic agent, dapsone, psoralen, an anti-malarial agent, an anti-viral agent, and an antibiotic.

10. (Original) The method of claim 8, wherein the immunomodulatory agent is selected from the group consisting of a proteinaceous agent, a peptide mimetic, an antibody, a nucleic acid molecule, a small molecule, an organic compound, an inorganic compound, methothrexate, leflunomide, cyclophosphamide, cytoxin, Immuran, cyclosporine A, minocycline, azathioprine, an antibiotic, methylprednisolone (MP), a corticosteroid, a steroid, mycophenolate mofetil, rapamycin, mizoribine, deoxyspergualin, brequinar, a malononitrioloamine, a T cell receptor modulator, and a cytokine receptor modulator.

11. (Currently amended) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin that has at least one of the following modifications compared to native erythropoietin i)-an erythropoietin that lacks 0, 1, 2, 3, 4, 5 , 6, 7, 8, 9, 10, 11, 12, or 13 sialic acid moieties;

ii) an erythropoietin that lacks a reduced number or no N-linked or lacks O-linked carbohydrates;

- iii) an erythropoietin having a reduced carbohydrate content by treatment of native erythropoietin with at least one glycosidase;
- iv) an erythropoietin having at least one or more oxidized carbohydrates;
- v) an erythropoietin comprising at least one or more oxidized carbohydrates which is that are chemically reduced;
- vi) an erythropoietin comprising at least one or more modified arginine residues;
- vii) an erythropoietin comprising at least one or more modified lysine residues or a modification of the N-terminal amino group of the erythropoietin molecule;
- viii) an erythropoietin comprising at least a one or more modified tyrosine residues;
- ix) an erythropoietin comprising at least a one or more modified aspartic acid or a glutamic acid residues;
- x) an erythropoietin comprising at least a one or more modified tryptophan residues;
- xi) an erythropoietin having at least one or more amino groups removed;
- xii) an erythropoietin comprising at least an opening of at least one of the cystine linkages in the erythropoietin molecule; and
- xiii) a truncation, truncated erythropoietin.

12. (Currently amended) The method of claim 8, wherein said tissue protective cytokine is asialoerythropoietin or phenylglyoxal-erythropoietin.

13. (Previously presented) The method of claim 8, wherein the tissue protective cytokine is capable of traversing an endothelial cell barrier.

14. (Original) The method of claim 13, wherein the endothelial cell barrier is selected from the group consisting of blood-brain barrier, blood-eye barrier, blood-testis barrier, blood-ovary barrier, and blood-uterus barrier.

15. (Currently amended) The method of claim 8, wherein the responsive cells, tissues, and/or organs in the mammal, are selected from the group consisting of neuronal cells, muscle cells, heart, lung, liver, kidney, small intestine, adrenal cortex, adrenal medulla, capillary cells, endothelial cells, testes, ovary, endometrial cells, and stem cells.

16. (Currently amended) The method of claim 8, wherein the responsive mammalian cells further comprise cells selected from the group consisting of photoreceptor

cells, ganglion cells, bipolar cells, horizontal cells, amacrine cells, Müller cells, myocardium cells, pace maker cells, sinoatrial node cells, sinus node cells, atrioventricular node cells, bundle of His cells, hepatocyte cells, stellate cells, Kupffer cells, mesangial cells, goblet cells, intestinal gland cells, enteral endocrine cells, glomerulosa cells, fasciculate cells, reticularis cells, chromaffin cells, pericyte cells, Leydig cells, Sertoli cells, sperm cells, Graffian follicle cells, primordial follicle cells, endometrial stroma cells, and endometrial cells.

17. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is asialoerythropoietin.

18. (Original) The method of claim 17, wherein said asialoerythropoietin is human asialoerythropoietin.

19. (Currently amended) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin with a reduced number or no N-linked carbohydrates.

20. (Currently amended) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin with a reduced number or no O-linked carbohydrates.

21. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin treated with at least one glycosidase.

22. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is periodate-oxidized erythropoietin.

23. (Original) The method of claim 22, wherein said periodate-oxidized erythropoietin is chemically reduced with sodium cyanoborohydride.

24. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin comprising a R-glyoxal moiety on the one or more arginine residues, wherein R is aryl or alkyl moiety.

25. (Original) The method of claim 24, wherein said erythropoietin is phenylglyoxal-erythropoietin.

26. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin in which at least one arginine residue is modified by reaction with a vicinal diketone selected from the group consisting of 2,3-butanedione and cyclohexanedione.

27. (Previously presented) The method of claim 8, wherein said tissue

protective cytokine is an erythropoietin in which at least one arginine residue is reacted with 3-deoxyglucosone.

28. (Currently amended) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin molecule comprising at least one biotinylated lysine or biotinylated N-terminal amino group.

29. (Currently amended) The method of claim [[28]]8, wherein said erythropoietin molecule is biotinylated erythropoietin.

30. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is a glucitolyt lysine erythropoietin or a fructosyl lysine erythropoietin.

31. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin having at least one carbamylated lysine residue.

32. (Original) The method of claim 31, wherein said carbamylated erythropoietin is selected from the group consisting of alpha-N-carbamoylerythropoietin; N-epsilon-carbamoylerythropoietin; alpha-N-carbamoyl, N-epsilon-carbamoylerythropoietin; alpha-N-carbamoylasialoerythropoietin; N-epsilon-carbamoylasialoerythropoietin; alpha-N-carbamoyl, N-epsilon-carbamoylasialoerythropoietin; alpha-N-carbamoylhyposialoerythropoietin; N-epsilon-carbamoylhyposialoerythropoietin; and alpha-N-carbamoyl, N-epsilon-carbamoylhyposialoerythropoietin.

33. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin in which at least one lysine residue is acylated.

34. (Original) The method of claim 33, wherein a lysine residue of said erythropoietin is acetylated.

35. (Original) The method of claim 34, wherein said acetylated erythropoietin is selected from the group consisting of alpha-N-acetylerythropoietin; N-epsilon-acetylerythropoietin; alpha-N-acetyl, N-epsilon-acetylerythropoietin; alpha-N-acetylasialoerythropoietin; N-epsilon-acetylasialoerythropoietin; alpha-N-acetyl, N-epsilon-acetylasialoerythropoietin; alpha-N-acetylhyposialoerythropoietin; N-epsilon-acetylhyposialoerythropoietin; and alpha-N-acetyl, N-epsilon-acetylhyposialoerythropoietin.

36. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin comprising a succinylated lysine residue.

37. (Original) The method of claim 36, where said erythropoietin is selected

from the group consisting of alpha-N-succinylerythropoietin; N-epsilon-succinylerythropoietin; alpha-N-succinyl, N-epsilon-succinylerythropoietin; alpha-N-succinylasialoerythropoietin; N-epsilon-succinylasialoerythropoietin; alpha-N-succinyl, N-epsilon-succinylasialoerythropoietin; alpha-N-succinylhyposialoerythropoietin; N-epsilon-succinylhyposialoerythropoietin; and alpha-N-succinyl, N-epsilon-succinylhyposialoerythropoietin.

38. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin with at least one lysine residue modified by a 2, 4, 6-trinitrobenzenesulfonic acid salt.

39. (Currently amended) The method[[s]] of claim 38, wherein the salt is 2, 4, 6-trinitrobenzenesulfonate sodium.

40. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin in which at least one tyrosine residue is nitrated and/or iodinated.

41. (Previously presented) The method of claim 8, wherein said tissue protective cytokine is an erythropoietin in which an aspartic acid and/or glutamic acid residue is reacted with a carbodiimide followed by reaction with an amine.

42. (Original) The method of claim 41, wherein said amine is glycinate.

43. (Previously presented) The method of claim 8, wherein the inflammation results from a disease condition or trauma.

44. (Currently amended) The method of claim [[43]]8, wherein the inflammation trauma is selected from the group consisting of angiitis, chronic bronchitis, pancreatitis, osteomyelitis, rheumatoid arthritis, glomerulonephritis, optic neuritis, temporal arteritis, encephalitis, meningitis, transverse myelitis, dermatomyositis, polymyositis, necrotizing fascilitis, hepatitis, and necrotizing enterocolitis.

45. (Previously presented) The method of claim 8, wherein the tissue protective cytokine inhibits inflammation resulting from cytokines produced by glial cells.

46. (Previously presented) The method of claim 8, wherein the inflammation is triggered by apoptosis.

47-52. (Cancelled).

53. (New) The method of claim 8, wherein said tissue protective cytokine is an alpha-N-carbamoyl, N-epsilon-carbamoylerythropoietin.

54. (New) The method of claim 8, wherein said tissue protective cytokine is non-erythropoietic.